REMARKS

The Office Action has subjected claims 1-31 to a ten-way restriction requirement, requiring the election of a single group from among Groups I - X, as defined therein. The restriction requirement further requires the election of single "composition" and "condition" species.

Applicants hereby elect, with traverse, the subject matter of Group I (claims 1-17 and 31, wherein Z = 0-12 carbon atoms) for further prosecution. Applicants hereby elect, with traverse, salicylihalamide A as the "composition" species, which claims 1-4 and 8-17 read on, and intra-organellar acidification of intracellular organelles as the "condition" species, which claims 1-12, 18-25 and 31 read on.

In support of the restriction requirement, the Office Action argues that Groups I-X are not so linked as to form a single general inventive concept on the grounds that Groups I-X allegedly lack the same or corresponding special technical features. However, the Office has failed to apply the proper standard for determining unity of invention.

PCT Rule 13.2 states:

> Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression 'special technical features' shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

In Markush practice, "the requirement of a technical interrelationship and the same or corresponding special technical features ... shall be considered to be met when the alternatives are of a similar nature." See M.P.E.P. § 1850. With regard to "similar nature," the M.P.E.P clearly states:

> When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:
>
> (A) All alternatives have a common property or activity; and
>
> (B)(1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or .... *Id.*

In the case at hand, all of the alternatives share a common property or activity, e.g., vacuolar-type (H+)-ATPase inhibitory activity. Applicants' specification makes this abundantly clear. See the specification, e.g., from p. 82, line 26, to p. 91, line 5.

Moreover, all of the recited compounds have a common structural feature that accounts not only for a significant portion of the molecule, but also plays an important role in biological activity. The specification, for example, at p. 20, lines 5-16, teaches:

> As indicated above, the compounds the present invention all share the structural component motif highlighted in Fig. 2. The compounds of the present invention are expected to possess vacuolar-type (H+)-ATPase inhibitory activity over a wide range of ring sizes, substitution patterns, structural variations, and the like. Indeed, compounds such as lobatamides A-F and salicylihalamides A and B exemplify compounds that incorporate the structural component motif highlighted in Fig. 2 and maintain potent vacuolar-type (H+)-ATPase inhibitory activity over a range of ring sizes (e.g., ranging from 12-15 members) and over a range of structural variations (e.g., variations in the structure of linker Z for salicylihalamide A versus lobatamide A).

The Office has produced no evidence whatsoever to contradict these findings. The factual assertions made by the Office Action arguing, e.g., "the types of atoms present in the lactone will strongly influence the nature of the compound used in the treatments" are entirely unsubstantiated by evidence and are contradicted by Applicants' own discovery. "The fact that the alternatives of a Markush grouping can be differently classified should not, taken alone, be considered to be justification for a finding of a lack of unity of invention." See M.P.E.P. §1850.

As such, it is improper for the Office to focus exclusively on differences in the linker Z, while ignoring the clear significance of the common structural feature shown, e.g., in Fig. 2, and shared by each and every one of the recited compounds. Indeed, not a single objection was ever raised concerning unity of invention in the international phase.

Moreover, the Office has failed to satisfy the two criteria for a proper restriction requirement between patentably distinct inventions, i.e.: (i) the inventions must be independent or distinct as claimed, and (ii) there must be a serious burden on the examiner if restriction is not required. See, e.g., M.P.E.P. § 803. "If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the

merits, even though it includes claims to independent or distinct inventions." *Id.* As such, *both* criteria (i) and (ii) must be met for a restriction requirement to be proper. In the case at hand, however, the Office has failed to so much as allege that there would be a serious burden on the Examiner if the election of inventions or species is not required.

Accordingly, the restriction requirement is improper and Applicants respectfully request that the restriction requirement be withdrawn so that all of the subject matter of Groups I-X is examined together. Even if the Examiner believes that a restriction requirement is necessary, requiring an election from among ten groups is believed to be excessive.

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, then the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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